

Application No. 10/699,991
Amendment dated January 2, 2008
Reply to Office action of July 2, 2007

AMENDMENT TO THE CLAIMS

The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method of treating muscle spasms comprising administering an effective anti-spasmodic amount of tizanidine ~~by a route of administration selected from the group consisting of buccal administration and sublingual administration and a pharmaceutically acceptable excipient, wherein the tizanidine is administered buccally or sublingually so that the tizanidine is absorbed through the mucosa lining of the mouth and tizanidine bioavailability AUC_{inf} is increased by 10% or more as compared to the AUC_{inf} of an immediate release tizanidine enteral dosage form absorbed through the gastro-intestinal track having an equivalent dose of tizanidine.~~

2. (Original) The method of claim 1 wherein the tizanidine is administered in a pharmaceutical composition or dosage form that releases 80% or more of the tizanidine in 20 minutes or less.

3. (Original) The method of claim 2 wherein the pharmaceutical composition or dosage form releases 80% or more of the tizanidine in 5 minutes or less.

Claims 4-6 Cancelled.

7. (Currently amended) The method of claim 1 ~~5~~ wherein the tizanidine bioavailability increase in bioavailability is an increase of 20% or more.

8. (Currently amended) The method of claim 1 ~~5~~ wherein the immediate release tizanidine enteral dosage form ~~tablet~~ comprises the excipients colloidal silicon dioxide, stearic acid, microcrystalline cellulose and anhydrous lactose.

9. (Currently amended) The method of claim 8 wherein the immediate release tizanidine enteral dosage form tablet is ZANAFLEX™.

10. (Previously amended) The method according to claim 1, wherein the effective anti-spasmodic amount of tizanidine reduces variations in the bioavailability of tizanidine between individuals in a patient population receiving tizanidine therapy.

Claims 11-17 cancelled.

18. (Currently amended) The method of claim 1 ~~17~~ wherein the reduction is about 30% or more.

19. (Withdrawn) A tizanidine pharmaceutical composition or oral dosage form especially adapted to release tizanidine in the mouth comprising tizanidine and a pharmaceutically acceptable carrier.

20. (Withdrawn) The tizanidine pharmaceutical composition or oral dosage form of claim 19 further comprising an acidulant.

21. (Withdrawn) The tizanidine pharmaceutical composition or oral dosage form of claim 20 wherein the acidulant is selected from the group consisting of ascorbic acid, benzoic acid, citric acid, fumaric acid, lactic acid, malic acid, sorbic acid and tartaric acid.

22. (Withdrawn) The tizanidine pharmaceutical composition or oral dosage form of claim 21 wherein the acidulant is citric acid.

23. (Withdrawn) The tizanidine pharmaceutical composition or oral dosage form of claim 19 wherein 80% of the tizanidine is released in twenty minutes or less after being taken into the mouth.

24. (Withdrawn) The tizanidine pharmaceutical composition or oral dosage form of claim 23 wherein 80% of the tizanidine is released in five minutes or less after being taken into the mouth.

25. (Withdrawn) The tizanidine pharmaceutical composition or oral dosage form of claim 19 that is a congealing liquid pharmaceutical composition comprising a hydrophilic polymer and a poly-protic hydrogen bonding cross-linking agent.

26. (Withdrawn) The tizanidine pharmaceutical composition of claim 25 wherein the cross-linking agent is tannic acid.

27. (Withdrawn) The tizanidine pharmaceutical composition of claim 25 wherein the hydrophilic polymer is selected from the group consisting of proteins, polysaccharides, cellulosic polymers and polyacrylates.

28. (Withdrawn) The tizanidine pharmaceutical composition of claim 27 wherein the protein is selected from the group consisting of gelatin, hydrolyzed gelatin, albumin and collagen.

29. (Withdrawn) The tizanidine pharmaceutical composition of claim 27 wherein the cellulosic polymer is selected from the group consisting of hydroxyethylcellulose, hydroxypropylcellulose and hydroxypropylmethylcellulose.

30. (Withdrawn) The tizanidine pharmaceutical composition of claim 27 wherein the polysaccharides is selected from the group consisting of pectin, carrageenan, alginic acid and their salts, guar gum and tragacanth gum.

31. (Withdrawn) The tizanidine pharmaceutical composition or oral dosage form of claim 19 that comprises a core tablet containing tizanidine sheathed in an annular body of pharmaceutical excipients.

32. (New) The method according to claim 1, wherein the tizanidine bioavailability has a relative standard deviation of AUC_{inf} that is 10% lower than a relative standard deviation of AUC_{inf} for the immediate release tizanidine enteral dosage form.

33. (New) The method according to claim 1, wherein the tizanidine bioavailability has a relative standard deviation of AUC_{inf} that is 20% lower than the relative standard deviation of AUC_{inf} for the immediate release tizanidine enteral dosage form.

34. (New) The method according to claim 1, wherein the tizanidine bioavailability has a relative standard deviation of AUC_{inf} that is 30% lower than the relative standard deviation of AUC_{inf} for the immediate release tizanidine enteral dosage form.

35. (New) The method according to claim 1, wherein the anti-spasmodic amount of tizanidine is in a dosage form having 2 mg to 8 mg of tizanidine.

36. (New) The method according to claim 1, wherein the anti-spasmodic amount of tizanidine is in a dosage form having 2 mg to 4 mg of tizanidine.

37. (New) The method according to claim 1, wherein the anti-spasmodic amount of tizanidine is in a dosage form that releases 80% or more of the tizanidine into the mouth in 20 minutes or less.

38. (New) The method according to claim 1, wherein the anti-spasmodic amount of tizanidine is in a dosage form that releases 80% or more of the tizanidine into the mouth in 5 minutes or less.

39. (New) The method according to claim 1 further comprising an acidulant in an amount to obtain saliva with a pH of 2 to 7.

40. (New) The method according to claim 39, wherein the acidulant is ascorbic acid, benzoic acid, citric acid, fumaric acid, lactic acid, malic acid, sorbic acid, or tartaric acid.

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41. (New) The method according to claim 39, wherein the acidulant is citric acid.